

## EPIDEMIC ENCEPHALITIS: INCLUDING A REVIEW OF 115 AMERICAN CASES.

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DURING the past three years, in the wake of a world-wide epidemic of respiratory disease, there have appeared an unusual number of cases presenting the symptomatology of a disseminated encephalitis. A brief study at this time of the etiology, pathology, symptomatology, prognosis and treatment as revealed by an analysis of 115 American cases, inclusive of 15 personal cases, should be of interest, for it would seem from a survey of the literature and from personal experience that epidemic encephalitis is being repeatedly misdiagnosed as poliomyelitis, botulism, brain abscess, cerebral hemorrhage, thrombosis, embolism, meningitis, acute paralysis agitans, etc., and that the data had not been at hand on which to evaluate the symptomatology of the disease.

The advent of a "new disease" naturally aroused the curiosity of students of medical history. It was soon learned that the supposed "new disease" was centuries old and had appeared repeatedly under different names, but with similar symptoms in association with previous respiratory epidemics. Crookshank<sup>1</sup> opens his article with an epigrammatic quotation from Bouvier,<sup>2</sup> written in 1837, which is worth repeating, and which summarizes, in an inimitable manner, the results of Crookshank's investigations into the history of the disease: "On l'a dit justement, les mêmes questions renaissent à chaque épidémie catarrhale et leurs solutions diverses se reproduisent chaque fois à peu près les mêmes." Different names have been applied in the past as in the present, but the symptoms were much the same. The first cases in the present epidemic were described by von Economo<sup>3</sup> in Austria in 1917; by Netter<sup>4</sup> in Paris in 1918; by Wilson<sup>5</sup> and others in England in 1918; by Tilney<sup>6</sup> and Riley in New York, and Bassoe<sup>7</sup> in Chicago, early in 1919.

<sup>1</sup> Boston Med. and Surg. Jour., 1919, clxxxii, 34.

<sup>2</sup> Ann. d'hyg. pub. et de méd. Legale, 1837.

<sup>3</sup> Wien. klin. Wchnschr., 1917, xxx, 581.

<sup>4</sup> Bulletin de l'académie de médecine, Paris, May, 1918, and November, 1918.

<sup>5</sup> London Lancet, 1918, ii, 91.

<sup>6</sup> Neurological Bulletin, 1919, vol. ii.

<sup>7</sup> Jour. Am. Med. Assn., 1919, lxxii, 971.

*Etiology.*—The cause of the disease is unknown and the opinions of those who have attempted etiological investigations are at variance. In 1917 von Wiesner<sup>8</sup> claimed to have produced a hemorrhagic encephalitis by inoculating into the brains of apes a diplococcus obtained from one of von Economo's cases, but without reproducing the histological pictures found in man. Marinesco<sup>9</sup> and McIntosh saw in and isolated from the meninges and pons two types of organisms, namely, a thick, Gram-positive, anaërobic bacillus which was pathogenic for mice and a diplococcus which was occasionally associated with the bacillus. Strauss,<sup>10</sup> at the Rockefeller Institute, reproduced the disease in apes with filtered nasopharyngeal secretions and maintained that the cause was a filtrable virus. May we not here again be up against the same *impasse* that has prevailed in poliomyelitis: the Flexner filtrable virus—globoid bodies—on the one hand and the Rosenow streptococcus with the "globoid bodies" considered merely as variants of a streptococcus, on the other hand?

One of us isolated a green streptococcus from the blood of a case (No. 12, Tables II and III) which was recovering from influenza with bronchopneumonia, and which was at the time developing a typical epidemic encephalitis with lethargy and diplopia. The organism was agglutinated by the patient's serum only and was not agglutinated by other sera. The patient's serum did not agglutinate laboratory strains of diplococci and streptococci. The organism had the cultural characteristics of the organism which was frequently isolated from the blood and lungs in the epidemic of influenza in Omaha in 1918 (Dunn<sup>11</sup>). The organism died out before animal experiments could be instituted and repeated cultures later failed to recover the organism. The immediate bearing of influenza on epidemic encephalitis is a moot question. In the 115 cases here analyzed 36 gave a history of a respiratory infection within one year (average time two months) prior to the onset of the encephalitis. The relative infrequency of encephalitis in a pandemic of influenza is noteworthy. On the contrary the appearance of encephalitic disease chiefly at the periods of a world-wide respiratory infection is suggestive. Draper<sup>12</sup> seemed inclined to assume that a close relationship exists between epidemic encephalitis and poliomyelitis, the former being a possible variant of the latter. It is to be noted that in 12 of our personal cases 5 gave a history of repeated severe tonsil infections; of the other infectious diseases, 2 had had typhoid, 2 diphtheria, 2 inflammatory rheu-

<sup>8</sup> Klin. Wehnschr., 1917, xxx, 933.

<sup>9</sup> L. G. B., London, 1918, p. 121.

<sup>10</sup> Jour. Am. Med. Assn., lxxii, 20, 1493; New York Med. Jour., 1919, cix, 772.

<sup>11</sup> Observations on an Epidemic of Bronchopneumonia in Omaha, Jour. Am. Med. Assn., December 28, 1918, p. 2128.

<sup>12</sup> L. G. B., London, 1918, No. 121, p. 62.

matism, 1 scarlet fever, 1 chorea, 1 pleurisy, 1 tuberculosis of the knee.

**Symptomatology.** The symptomatology of epidemic encephalitis is protean. When one considers that it is the brain-stem—the great switchyard of the central nervous system—which is the site of predilection of the virus the multiplicity of symptom complexes is explained. Even microscopic lesions in such an area as the mesencephalon may be fraught with much symptomatic import. All parts of the brain-stem and cerebrum, however, are open to attack. We have found it useful from a clinical standpoint to arrange the more or less characteristic symptoms in groups or types: (1) Polioencephalitic; (2) lethargic; (3) Parkinsonian; (4) cataleptic; (5) meningitic; (6) cerebral; (7) polyneuritic; (8) myelitic. We have endeavored to place these groups on a pathological and anatomical basis. We confess that the grouping is artificial, and that, on account of the multiplicity and disseminated character of the lesions it cannot be a hard and fast one, but in the study and recognition of cases we have found it helpful. The classification has been arranged from an analysis of the symptoms of 115 cases, with acknowledgment to MacNalty,<sup>13</sup> Tilney and Riley (*loc. cit.*) and others. The syndromes always overlap, so that a case may easily find itself in two or more groups. For example, J. C. (Case No. 9, Tables II and III) could have been placed at different times in either of two groups: In the cerebral group on account of Jacksonian epilepsy, motor aphasia and right-sided spasticity; in the agitans group on account of tremor, spasticity and the Parkinsonian mask. Careful correlation of symptom groupings with subsequent pathological study may throw some light on cerebral localization and on the function of the “dark” areas of the central nervous system. Five of the 15 personal cases were classified as polioencephalitic (1 superior); 3 lethargic; 1 Parkinsonian; 1 meningitic; 4 cerebral (2 convulsive, 1 psychotic, 1 epileptomaniacal), 1 polyneuritic. It must be emphasized that the group to which a given case is assigned depends greatly on the time in the course of the disease at which the patient is grouped. At one period a case may fall clearly into the polioencephalitic at a later period into the lethargic group. We have excluded a poliomyelitic group, for neither in our own cases nor in the literature do we find any cases which are sufficiently frank to be called poliomyelitic. Tilney and Riley’s (*loc. cit.*) case is exceptional. The lethargy in this case would not seem typical, and one case is not sufficient grounds for a separate type without pathological corroboration. We feel that the posterior poliomyelitic type can quite well be classified, temporarily at least, as polyneuritic.

<sup>13</sup> L. G. B., London, 1918, No. 121.

TABLE I.—SYMPTOMATOLOGY. CLASSED ANATOMICALLY.

| Type.                                 | Symptom.  | 100 cases. | 15 cases. | Part.   |
|---------------------------------------|---|------------|-----------|---|
| Polioencephalitic<br>Ophthalmoparetic | Cranial nerve palsies:                                | ..         | ..        | Midbrain,<br>pons and<br>medulla.                               |
|                                       | III . . . . .   | 60         | 6         |   |
|                                       | IV . . . . .  | 2(?)       | 0         |   |
|                                       | V . . . . .   | 7          | 3         |   |
|                                       | VI . . . . .  | 34         | 6         |   |
|                                       | VII . . . . .   | 12         | 5         |   |
|                                       | VIII . . . . .  | 4          | 2         |   |
|                                       | IX . . . . .  | 2          | 0         |   |
|                                       | X . . . . .   | 1          | 0         |   |
|                                       | XI . . . . .  | 0          | 0         |   |
|                                       | XII . . . . .   | 11         | 2         |   |
|                                       | Eyes:   |            |           |   |
| Lethargy                              | Diplopia . . . . .                                    | 50         | 8         | Pituitary,<br>thalamus,<br>iter and<br>cerebrum.<br>Cerebellum. |
|                                       | Anisocoria . . . . .                                  | 25         | 4         |   |
|                                       | Ptosis . . . . .                                      | 20         | 6         |   |
|                                       | Lack of light and accommoda-<br>tion reflex . . . . . | 12         | 4         |   |
|                                       | Sluggish pupils . . . . .                             | 20         | 4         |   |
|                                       | Retinal changes . . . . .                             | 10         | 2         |   |
|                                       | Swallowing . . . . .                                  | 13         | 0         |   |
|                                       | Vomiting . . . . .                                    | 8          | 1         |   |
|                                       | Polypnea . . . . .                                    | 1          | 2         |   |
|                                       | Lethargy . . . . .                                    | 69         | 10        |   |
|                                       | Insomnia . . . . .                                    | 16         | 4         |   |
| Cataleptic                            | Catalepsy . . . . .                                   | 20         | 6         | Meninges.   |
|                                       | Vertigo . . . . .                                     | 19         | 5         |   |
|                                       | Nystagmus . . . . .                                   | 17         | 1         |   |
| Meningeal                             | Ataxia . . . . .                                      | 4          | 2         | Meninges.   |
|                                       | Headache . . . . .                                    | 47         | 10        |   |
|                                       | Rigidity neck . . . . .                               | 12         | 1         |   |
|                                       | Delirium . . . . .                                    | 24         | 6         |   |
|                                       | Kernig . . . . .                                      | 3          | 3         |   |
| Paralysis agitans                     | Tache . . . . .                                       | 1          | 0         | Lenticular<br>nucleus.  |
|                                       | Parkinsonian mask . . . . .                           | 9          | 3         |   |
|                                       | Spasticity . . . . .                                  | ..         | 4         |   |
| Myelitic                              | Festination . . . . .                                 | 3          | 0         | Cord  |
|                                       | Tremor . . . . .                                      | 30         | 5         |   |
|                                       | Bladder . . . . .                                     | 15         | 4         |   |
|                                       | Reflexes disturbed . . . . .                          | 25         | 7         |   |
|                                       | Babinski . . . . .                                    | 14         | 7         |   |
| Epileptomaniacal                      | Reflexes absent . . . . .                             | 2          | 2         | Cerebrum.   |
|                                       | Clonus . . . . .                                      | 5          | 4         |   |
|                                       | Convulsions . . . . .                                 | 0          | 2         |   |
|                                       | Paralyses . . . . .                                   | 0          | 1         |   |
| Psychotic                             | Asynergies . . . . .                                  | 20         | 0         | Cerebrum.   |
|                                       | Epileptiform attacks . . . . .                        | ..         | 3         |   |
|                                       | Hallucinations . . . . .                              | ..         | 3         |   |
|                                       | Illusions . . . . .                                   | ..         | 3         |   |
|                                       | Depression . . . . .                                  | 9          | ..        |   |
| Polyneuritic                          | Delirium . . . . .                                    | 24         | 7         | Cerebrum.   |
|                                       | Pain in extremities . . . . .                         | 23         | 3         |   |
|                                       | Sensation disturbed . . . . .                         | ..         | 1         |   |
|                                       | Paresthesias . . . . .                                | 6          | 3         |   |
|                                       | General symptoms:                                     |            |           |   |
|                                       | Epistaxis . . . . .                                   | 1          | 1         |   |
|                                       | Cervical adenitis . . . . .                           | ..         | 2         |   |
|                                       | Tachycardia . . . . .                                 | ..         | 1         |   |
|                                       | Weight loss . . . . .                                 | ..         | 5         |   |
|                                       | Appetite increased . . . . .                          | ..         | 6         |   |
|                                       | Fever . . . . .                                       | 43         | 13        |   |
|                                       | Perspiration . . . . .                                | 6          | 15        |   |
|                                       | Hiccough . . . . .                                    | 5          | 0         |   |
|                                       | Tears . . . . .                                       | 4          | 0         |   |

Table I has been made to show the relative frequency of individual symptoms and their grouping. This table is instructive from the symptom incidence as well as from the localization standpoint. The anatomical localization of symptoms in some instances is far from settled. Lethargy is attributed to pituitary involvement by Cushing<sup>14</sup> and Climenko<sup>15</sup> and to the thalamus by von Economo (*loc. cit.*), MacNalty (*loc. cit.*) and Flexner.<sup>16</sup> We have assigned catalepsy to the cerebellum because it is a manifestation of disturbance in that extrapyramidal muscle tonus controlling apparatus of which the cerebellum forms an important part. Vertigo, nystagmus and ataxia are grouped under the cerebellum also because they arise as frequently in cerebellar as in disturbances elsewhere. Disturbed bladder and deep and superficial reflexes are attributed to the cord because they occur in cord diseases, but with full realization that some of them occur quite as frequently from lesions elsewhere. The groups or types, as shown in Table I, are useful merely in calling attention to symptom-complexes and in facilitating their recognition.

**Special Symptoms.** Certain of the more prominent symptoms should receive comment. The incidence of what we consider the less important symptoms can be seen by consulting Table I.

**Ocular Disturbances.** Disturbance in the third and sixth nerves is far and away the most common symptom occurring in epidemic encephalitis. In the 115 cases third nerve palsies were present in 63 cases and sixth nerve in 39. Diplopia was the initial symptom in 19 cases and was recorded in 55 cases. Ptosis was present 21 times. Diplopia is often an evanescent and baffling symptom, for although the patient may maintain that he sees double, yet the oculist cannot demonstrate the muscles involved. We believe that this symptom is more common than the statistics would indicate, because invariably in our own cases, when the question was brought up squarely to the patient or to the relatives the presence of visual disturbances was substantiated. The absence of the fourth nerve involvement is striking in spite of the close anatomical proximity of its nucleus to that of the third. Is this due to its short and protected course on the dorsum of the brainstem? *In what may be considered as a diagnostic triad of the disease viz., (1) ocular symptoms, (2) lethargy and (3) a negative or typically atypical spinal fluid, ocular symptoms hold first place.*

**Other Cranial Nerves.** The sensory portion of the fifth was involved 9 times in 115 cases. Apparently the motor portion of the fifth is rarely involved, and may not this be explained, in some instances at least, by its long mesencephalic sensory root which extends along the floor of the iter in close proximity to the nuclei of the third

<sup>14</sup> Diseases of the Pituitary, Philadelphia, 1912, pp. 101-102.

<sup>15</sup> New York Med. Jour., March 27, 1920.

<sup>16</sup> Jour. Am. Med. Assn., March 27, 1918.

nerve which are so commonly involved? In one of our cases the onset was associated with pain on the right side of the head and face, which soon shifted to the left side, and which was so severe that morphin was required. The patient did not sleep for seven days. Later a seventh nerve paralysis developed. As the pain subsided lethargy appeared. The development of a corneal ulcer on the left side, a left peripheral seventh paralysis, an involvement of the left chorda tympani and a left nerve deafness in this case are noteworthy. In the presence of the above symptoms, and with a spinal fluid showing 24 cells per cubic millimeter, globulin plus 2, a mild paretic gold chloride curve, negative cultures and smears and a negative Wassermann in both spinal fluid and blood, a *localized meningitis of unknown etiology* was assumed until lethargy appeared. This case would be explained by the meningoradiculitis conception recently advanced by Bassoe.<sup>17</sup> Fifteen of the cases had paralysis of the seventh nerve. The paralysis was generally peripheral in type and unilateral. The tendency of seventh nerve paralysis is to clear up slowly, requiring from four to five months. Involvements of the other cranial nerves (first, second, ninth, tenth, eleventh and twelfth) seems of minor diagnostic significance (13 cases out of 115). (See Table I.)

*Polypnea* occurred in 3 cases, 2 of them in our own series. In one of our cases (No. 5) a respiratory state of 60, which seemed to be of respiratory center origin, was maintained for thirty-six hours. The respirations in the other case (No. 10) were 80 to 100 per minute; they suggested irregular diaphragmatic and abdominal spasms (myoclonus) and occurred in attacks which were associated with extreme suffering, necessitating the use of morphin. This symptom, although rare, merits special attention, because when present it dominates the clinical picture.

*Lethargy* occurred in 79 cases and was the first symptom noted in 34 cases. It was preceded by insomnia in 4 cases. The degree of lethargy was variable. In extreme cases it may approximate a coma vigil. Usually the patients can be aroused and appear dazed as if awakening from a deep sleep. The patients, when aroused, eat and answer questions, but soon relapse into their stupor. The dazed, blank, expressionless stare is quite characteristic. The lethargy in most instances does not differ from a normal deep sleep, but on awakening a normal expression is absent. The patients are negativistic and their faces are dead. The lights of intelligence and interest are out or burn low.

*Catalepsy* and *catatonia* would seem to be more common than it appears from the literature, occurring in 6 out of 15 cases in our personal series and in only 20 out of the 100 cases collected from American literature. Increased muscle rigidity is common and *flexibilitas cerea* was noted 4 times in our 15 cases.

<sup>17</sup> The Delirious and Meningoradicular Type of Epidemic Encephalitis, Jour. Am. Med. Assn., April 10, 1920, lxxiv, 1009.

TABLE II.—GENERAL SYMPTOMS IN EPIDEMIC ENCEPHALITIS.

| Sex, age, name, date.                           | General.   | Medulla. | Cerebrum, iter.  | Cerebellum.                      | Meninges.                             | Lenticular nucleus.                     | Cord periphery.  |
|---|--|----------|--|----------------------------------|---------------------------------------|---|--|
| 1.—U. H. (M.),<br>53 years<br>Feb. 13, 1920     | Weight loss; fever; perspire;<br>chilly                                | ...      | Apathy; insomnia   | Nystagmus<br>vertigo             | Headache                              | Mask.                                   | Oppenheim left; Gordon left.   |
| 2.—F. P. K. (M.),<br>40 years<br>Feb. 4, 1920   | Weight loss; nosebleed; fever  | ...      | Drowsy; insomnia   | ...                              | Headache                              | ...                                     | Knee-jerks, plus 3; Romberg.   |
| 3.—F. S. B. (M.),<br>36 years<br>Jan. 8, 1920   | Weight loss  | ...      | .....  | Vertigo                          | Headache                              | ...                                     | Oppenheim; sphincter loss;<br>numbness in hands; chest;<br>clonus; knee-jerks.<br>Pain in right arm.   |
| 4.—M. H. (F.),<br>20 years<br>Jan. 23, 1920     | Temperature 100°; cervical<br>nodes enlarged                           | ...      | Insomnia; nervous delirium   | ...                              | Headache;<br>photophobia;<br>Kernig   | ...                                     | ...  |
| 5.—O. S. H. (M.),<br>50 years<br>Feb. 27, 1920  | Grippe, 101°   | ...      | Lethargy; delirium   | ...                              | ....                                  | ...                                     | ...  |
| 6.—J. D. (M.),<br>50 years<br>Oct. 19, 1919     | .....  | Polypnea | Coma; delirium; lethargy;<br>clonus arms                             | Nystagmus;<br>vertigo            | Headache                              | ...                                     | Twitching arms; abdominal<br>clonus; Oppenheim right.  |
| 7.—J. S. (F.),<br>5 years<br>May 23, 1919       | Chilly; fever; adenitis; scal-<br>ing bands; nausea; perspi-<br>ration | ...      | Convulsions; Jacksonian epi-<br>lepsy; coma                          | ...                              | Headache;<br>photophobia<br>irritable | ...                                     | Twitching; Oppenheim; Bab-<br>inski; knee-jerks.   |
| 8.—H. H. (M.),<br>44 years<br>Apr. 3, 1919      | Perspiration; fever; carphol-<br>ogia; appetite increased              | ...      | Lethargy; delirium; sensa-<br>tion?                                  | Catalepsy                        | Headache;<br>rigid neck               | Tremor;<br>mask;<br>spastic             | Babinski.  |
| 9.—J. C. (M.),<br>55 years<br>Aug. 20, 1919     | Dyspnea; aphonia; perspi-<br>ration                                    | ...      | Right-hand spasm; lethargy;<br>motor aphasia; Jacksonian<br>epilepsy | Vertigo;<br>ataxia;<br>catalepsy | Headache                              | Scanning<br>speech;<br>mask;<br>spastic | Babinski in right; ankle-<br>clonus; right arm reflex,<br>plus 2.  |
| 10.—H. W. (M.),<br>46 years<br>Feb. 17, 1920    | Fever  | Polypnea | Delirium; hallucinations;<br>illusions                               | ...                              | Headache;<br>Kernig                   | ...                                     | Pain in legs; Oppenheim; in-<br>continence; Babinski in<br>right; knee-jerks and ankle-<br>jerks.<br>Oppenheim; Babinski; Gor-<br>don; clonus. |
| 11.—E. L. C. (M.),<br>18 years<br>Jan. 27, 1920 | Perspiration; appetite in-<br>creased                                  | ...      | Illusions; lethargy; insom-<br>nia; loss of memory                   | Catalepsy                        | Photophobia                           | Spastic                                 | Babinski.  |
| 12.—Mrs. B. (F.),<br>45 years<br>Feb. 2, 1920   | Tachycardia; nephritis; in-<br>fluenza                                 | ...      | Illusions; delirium; lethargy;<br>hallucinations                     | Catalepsy                        | Kernig                                | Tremor                                  | Incontinence.  |
| 13.—M. M. (M.),<br>34 years<br>Apr. 1, 1919     | Chills; fever; carphologia   | ...      | Lethargy; delirium   | Vertigo                          | Photophobia;<br>headache              | ...                                     | ...  |
| 14.—I. F.<br>Feb. 1, 1920                       | Fever; pneumonia   | ...      | Lethargy   | Right<br>tremor                  | ....                                  | ...                                     | Babinski in right; arm-clonus<br>in right.   |
| 15.—G. V. (M.),<br>25 years<br>Jan. 25, 1920    | Perspiration; fever  | ...      | Jacksonian epilepsy  | ...                              | ...                                   | ...                                     | ...  |

TABLE III.—CRANIAL NERVE SYMPTOMS IN EPIDEMIC ENCEPHALITIS.

| Name, sex, age, date.                           | N. II.    | Nerve III.   |                |                             |  | Photo-phobia. | IV and V.                    | VI.      | VII. | VIII. | IX. | X.            | XI. | XII. |
|---|-----------|--------------|----------------|-----------------------------|--|---------------|------------------------------|----------|------|-------|-----|---------------|-----|------|
|   |           | Pto-<br>sis. | Diplo-<br>pia. | Light and<br>accommodation. | Pupil.   |               |                              |          |      |       |     |               |     |      |
| 1.—U. H. (M.),<br>55 years<br>Feb. 3, 1920      | 0         | Bilateral    | plus           | Inability to read           | Left dilated                                       | plus          | Pain: tremor<br>in face<br>0 | 0        | Lt.  | Lt.   | 0   | Pulse,<br>100 | 0   | Lt.  |
| 2.—F. P. K. (M.),<br>40 years<br>Feb. 4, 1920   | Edema     | 0            | plus           | ....                        | ....   | plus          | 0                            | plus rt. | 0    | 0     | 0   | 80            | 0   | 0    |
| 3.—F. S. B. (M.),<br>56 years<br>Jan. 8, 1920   | 0         | 0            | plus           | ....                        | ....   | plus          | Pain in<br>face              | plus rt. | 0    | Rt.   | 0   | ...           | 0   | 0    |
| 4.—M. H. (F.),<br>20 years<br>Jan. 23, 1920     | 0         | Rt.          | 0              | ....                        | ....   | plus          | Pain in<br>face              | 0        | Rt.  | 0     | 0   | 90            | 0   | 0    |
| 5.—O. S. H. (M.),<br>50 years<br>Feb. 27, 1920  | Edema     | 0            | plus           | ....                        | ....   | 0             | 0                            | plus lt. | 0    | 0     | 0   | 76            | 0   | 0    |
| 6.—J. D. (M.),<br>50 years<br>Oct. 19, 1919     | left<br>0 | Rt.          | plus           | Absent                      | ....   | 0             | 0                            | plus rt. | Rt.  | 0     | 0   | 90            | 0   | Lt.  |
| 7.—J. S. (F.),<br>5 years<br>May 23, 1919       | 0         | 0            | 0              | ....                        | Right<br>dilated<br>irregular<br>Middlat-<br>ation | plus          | 0                            | 0        | 0    | 0     | 0   | 150           | 0   | 0    |
| 8.—H. H. (M.),<br>44 years<br>Apr. 3, 1919      | 0         | 0            | 0              | ....                        | ....   | plus          | 0                            | 0        | 0    | 0     | 0   | 100           | 0   | 0    |
| 9.—J. C. (M.),<br>55 years<br>Aug. 20, 1919     | 0         | 0            | 0              | ....                        | Sluggish   | 0             | 0                            | 0        | 0    | 0     | 0   | 72            | 0   | 0    |
| 10.—H. W. (M.),<br>46 years<br>Feb. 17, 1920    | 0         | 0            | 0              | ....                        | Middlat-<br>ation                                  | plus          | 0                            | 0        | 0    | 0     | 0   | 90            | 0   | 0    |
| 11.—E. L. C. (M.),<br>18 years<br>Jan. 27, 1920 | 0         | 0            | 0              | ....                        | Middlat-<br>ation                                  | plus          | 0                            | 0        | 0    | 0     | 0   | 60            | 0   | 0    |
| 12.—Mrs. B. (F.),<br>45 years<br>Feb. 2, 1920   | 0         | 0            | 0              | ....                        | ....   | 0             | ...                          | 0        | Rt.? | 0     | 0   | ...           | 0   | 0    |
| 13.—M. M. (M.),<br>34 years<br>Apr. 1, 1919     | 0         | Rt.          | plus           | No accommoda-<br>tion       | ....   | plus          | 0                            | plus rt. | 0    | 0     | 0   | ...           | 0   | 0    |
| 14.—I. I. (M.),<br>25 years<br>Jan. 25, 1920    | 0         | Rt.          | plus           | No accommoda-<br>tion       | ....   | plus          | 0                            | plus     | 0    | 0     | 0   | ...           | 0   | 0    |
| 15.—V. V. (M.),<br>25 years<br>Jan. 25, 1920    | 0         | Lt.          | plus           | ....                        | Both<br>dilated                                    | 0             | 0                            | 0        | Rt.  | 0     | 0   | ...           | 0   | 0    |



*Headache* appeared as an initial symptom in 12 cases and was present in 54 cases. It must have been confused in many instances with sensory fifth nerve involvement. Sore scalp was a common complaint. Hyperesthesias and anesthetics have been occasionally described. Severe toxic headaches occur at the onset and rapidly disappear as lethargy supervenes, unless meningeal involvement is present. Headaches in the early stages may be due in some instances to ocular disturbances, such as diplopia, photophobia, etc.

*Rigidity of the neck*, if present, is not, as a rule, marked. Confusion may be easily avoided in regard to this symptom if one remembers that increased muscle tonus is commonly a part of the picture of epidemic encephalitis. If marked rigidity of the neck, with Kernig's or Brudzinski's signs, exist, meningitis is to be looked for.

*Tremor* was present in 35 cases. The descriptions given are usually vague and inaccurate. The tremor is most commonly coarse, often unilateral and not intentional. Tremor, or twitching of the abdominal muscles, has occasionally been reported in the literature (Reilly<sup>18</sup> and Bassoe, *loc. cit.*). We have seen this symptom in 2 cases. Facial twitching preceding a facial paralysis by several days was noted twice in our series.

*Disturbances in reflexes* are not common or uniform. Four cases in the series showed an absence of deep reflexes or a hyporeflexia, 2 of which cases were fatal. The knee-jerks were as often increased as absent. Babinski's sign was present only 18 times and usually transitory. Oppenheim's sign was present in 5 of our 15 cases. Ankle clonus was present in 8 of the 115 cases. In 31 cases some changes in reflexes were noted. It would seem that the greatest value of a change in reflexes was to exclude functional disease of the nervous system, which may be difficult at the first examination. *Peripheral pain* is a common symptom, 26 cases out of the 115. It has not received the attention that it should, for we found it in 6 out of our 15 cases. The pain is commonly described as cramp-like, burning, boring, shooting, occasionally associated with paresthesia, and is of the neuritic type. We are convinced that it will be frequently found if inquired into. It is probably of meningitic, radicular or neuritic origin. If cases of present-day obscure pain, neuritic in character, are carefully investigated we feel sure that some of them will fall into the class of mild cases of epidemic encephalitis.

*Perspiration*. Sweating, judging from our cases, is very common, from the literature, very rare. Though present in all of our cases it was reported only 6 times in the 100 cases from the literature. In 6 of our cases it took the form of night-sweats, which were a

<sup>18</sup> Hitherto Undescribed Signs in Diagnosis of Lethargic Encephalitis, Jour. Am. Med. Assn., 1920, lxxiv, 735.

source of anxiety to the patient or to relatives. According to Crookshank (*loc. cit.*) "the sweating sickness" which was prevalent in England in the seventeenth and eighteenth centuries is the same disease which is now prevalent as epidemic encephalitis.

*Fever.* The average maximum temperature was 102° F. except in lethal cases, in which a prelethal rise to 105° or 106° was common. Complete absence of fever was noted in 50 of the cases. In all events fever was usually transitory and prevailed only for short periods of the disease.

**Laboratory Findings.** Leukocyte counts were reported on 36 of the 100 cases. They averaged 10,200 white cells, 72 per cent. of which were polynuclears. The highest count was 22,000. Of 25 counts in our series of 15 cases the average leukocyte count was 10,200, of which 71 per cent. were polynuclears. The red counts and the hemoglobin percentages were approximately normal. The Wassermann test was uniformly negative. Blood cultures were negative except in one case of the 15 series, from which a green streptococcus, which was agglutinated by the patient's serum, was isolated. The urine examinations showed only the usual changes encountered in acute infections.

TABLE IV.—CEREBROSPINAL FLUIDS.

| Name.              | Day of disease. | Appearance. | Pressure. | Cells. | Globulin. | Wassermann. | Gold chloride. |
|--------------------|-----------------|-------------|-----------|--------|-----------|-------------|----------------|
| 11.—E. L. C. . .   | 18              | Clear       | plus 1    | 2 m.   | 0         | 0           | 112321000      |
| 11.—E. L. C. . .   | 38              | Clear       | plus 1    | 2 m.   | 0         | 0           |                |
| 11.—E. L. C. . .   | 60              | Clear       | 0         | 2 m.   | 0         | 0           | 122210000      |
| 10.—H. W. . . .    | 30              | Clear       | plus 1    | 3      | 0         | 0           |                |
| 9.—J. C. . . . .   | 90              | Clear       | 0         | 0      | 0         | 0           |                |
| 8.—H. H. . . . .   | 35              | Clear       | plus 1    | 16 m.  | ..        | 0           |                |
| 8.—H. H. . . . .   | 41              | Clear       | plus 1    | 12 m.  | ..        | 0           |                |
| 7.—J. S. . . . .   | 50              | Clear       | 0         | 0      | 0         | 0           | 1355542000     |
| 6.—J. D. . . . .   | 10              | Clear       | plus 2    | 3 m.   | 0         | 0           |                |
| 4.—M. H. . . . .   | 15              | Clear       | plus 1    | 3 m.   | 0         | 0           | 0122300        |
| 1.—U. H. . . . .   | 35              | Clear       | plus 2    | 24 m.  | plus 2    | 0           | 12220000       |
| 1.—U. H. . . . .   | 49              | Clear       | plus 1    | 11 m.  | 0         | 0           | 112211000      |
| 1.—U. H. . . . .   | 63              | Clear       | plus 1    | 3 m.   | 0         | 0           | 1222110000     |
| 3.—F. S. B. . . .  | 70              | Clear       | plus 1    | 13 m.  | 0         | 0           | 00011111000    |
| 2.—F. P. K. . . .  | 70              | Clear       | plus 1    | 3      | plus 1    | 0           | 1111100000     |
| 13.—M. M., S. Dak. | ..              | Clear       | plus 1    | ..     | plus 1    | 0           |                |
| 14.—Iowa . . . .   |                 |             |           |        |           |             |                |
| 12.—Mrs. B. . . .  | 21              | Clear       | plus 1    | 3      | 0         | 0           |                |
| 15.—G. I. . . . .  | 35              | Clear       | plus 1    | 0      | plus 1    | 0           | 0122211234     |

*Spinal Fluids.* This table gives the findings in nineteen spinal fluids obtained from the personal series of 15 cases (Table IV). The average day of disease on which the taps were made was the thirty-sixth. The earliest tap was made on the tenth day and the latest on the ninetieth day. The fluids were all clear and came with increased pressure in 7 instances. The average number of

cells was 9 per cubic millimeter. The highest cell count was 24. The cells were chiefly mononuclears. Globulin (Nonne-Apelt test) was increased in 4 cases. All the Wassermann tests were negative. The gold chloride was mildly luetic in 7 out of 11 examinations in which this test was made.

In Table V are 64 spinal fluid examinations collected from the 100 cases in the literature. The average number of cells in the series was 16 mononuclears per cubic millimeter. The pressure was increased in only 10 per cent. The globulin test was positive in over 50 per cent.

**Pathology.** In a region so difficult to examine as the brain-stem it is remarkable how definite a pathological picture has been set forth by the investigators. Marinesco, McIntosh, Tilney and Riley and Bassoe have given us the most information. In the only case in our series which came to autopsy the congestion of the frontal lobes, the patchy edematous meninges and the marked thickening of the basilar meninges were apparent in the gross. On macroscopic sections the brain-stem substance was soft and numerous punctate hemorrhages were found in the mesencephalic and thalamic areas. Microscopic sections showed marked edema of the peri-aqueductal gray matter, with small hemorrhages into the white and gray matter. The venules showed perivascular infiltration, with lymphocytes, plasma cells and mononuclears. Many of the vessels were thrombosed. Neither neuronophagia nor satellitosis were present. The chief pathological changes as shown in the literature may be summed up as follows: (1) Meningeal edema and thickening; (2) softening and congestion of both gray and white matter of the brain and pituitary gland; (3) punctate hemorrhages in mesencephalon and thalamus and basal ganglia; (4) thrombosis of small vessels; (5) perivascular infiltration of small vessels of the brain-stem; (6) edema of the mesencephalic area.

**Prognosis.** Out of Barker's 8 cases none died; 6 of von Economo's 11 died; 7 of Netter's 15 cases died; 2 of Wilson's 13 cases died; 5 of Tilney's 20 cases died; 31 of the 100 cases collected from the American literature died. Of our series 4 out of 15 died, 4 recovered wholly in one and a half to four months and 7 at the end of two or three months had fifth, sixth, seventh and eighth nerve disturbances; one still had pain in the arm after two months. Disturbances in cerebation and equilibrium took on the average three or four months to clear up entirely. Facial nerve palsies lasted four or five months. Asthenia, depression and dizziness persisted seven months as an average. The fatal cases generally terminated in the first few days or weeks of the disease, so that the longer the course of the case the better the chances of recovery. The four deaths in our series resulted in three, five, six and sixteen weeks respectively.

TABLE V.—CEREBROSPINAL FLUIDS, 100 CASES.

|        | Appearance. | Pressure. | Cells.    | Globulin. | Wassermann. | Gold chloride. |
|--------|-------------|-----------|-----------|-----------|-------------|----------------|
| 1 . .  | ...         | ...       | 30 m.     | plus 4    | 0           |                |
| 2 . .  | Clear       | ...       | 11 m.     | plus 4    | 0           |                |
| 3 . .  | Clear       | ...       | 133 m.    | plus 4    | 0           | Luetic curve.  |
| 4 . .  | Clear       | ...       | 30 m.     | plus 1    | 0           |                |
| 5 . .  | Clear       | ...       | 2 to 7 l. | plus 1    | 0           | Paretic curve. |
| 6 . .  | Clear       | plus 1    | 48 m.     | plus 3    | 0           |                |
| 7 . .  | Clear       | plus 1    | 6 l.      | 0         | 0           |                |
| 8 . .  | Clear       | ...       | ...       | ...       | 0           |                |
| 9 . .  | Clear       | ...       | ...       | ...       | 0           |                |
| 10 . . | Clear       | ...       | 0         | 0         | 0           |                |
| 11 . . | Bloody      | ...       | 23 l.     | 0         | 0           |                |
| 12 . . | Clear       | ...       | 3 l.      | 0         | 0           |                |
| 13 . . | Clear       | ...       | 7 l.      | 0         | 0           |                |
| 14 . . | Clear       | ...       | 0 l.      | 0         | 0           |                |
| 15 . . | Clear       | ...       | 0         | 0         | 0           |                |
| 16 . . | Clear       | plus 2    | 0         | 0         | 0           |                |
| 17 . . | Clear       | ...       | 4 l.      | 0         | 0           |                |
| 18 . . | Clear       | ...       | 85 l.     | 0         | 0           |                |
| 19 . . | Clear       | ...       | 20 l.     | 0         | 0           |                |
| 20 . . | Clear       | ...       | 64 l.     | 0         | 0           |                |
| 21 . . | Clear       | ...       | 66 l.     | 0         | 0           |                |
| 22 . . | Clear       | ...       | 7 l.      | 0         | 0           |                |
| 23 . . | Clear       | ...       | 29 l.     | 0         | 0           |                |
| 24 . . | Clear       | ...       | 4 l.      | plus      | 0           | 23433321100    |
| 25 . . | Clear       | ...       | 7 l.      | 0         | 0           |                |
| 26 . . | Clear       | ...       | 9 l.      | plus      | 0           | 1221110000     |
| 27 . . | Clear       | plus 1    | 26 l.     | plus      | 0           | 0112111000     |
| 28 . . | Clear       | ...       | 25 l.     | plus      | 0           |                |
| 29 . . | Clear       | ...       | ...       | 0         | 0           |                |
| 30 . . | Clear       | ...       | 4 l.      | plus      | 0           |                |
| 31 . . | Clear       | ...       | 9 l.      | plus      | 0           | 0122110000     |
| 32 . . | Clear       | ...       | 10 l.     | plus      | 0           | 1222110000     |
| 33 . . | Clear       | ...       | 5 l.      | 0         | 0           |                |
| 34 . . | Clear       | plus 1    | 12 l.     | 0         | 0           |                |
| 35 . . | Clear       | ...       | ...       | 0         | 0           |                |
| 36 . . | Clear       | plus 1    | 35 l.     | plus 1    | 0           |                |
| 37 . . | Clear       | ...       | ...       | ...       | 0           |                |
| 38 . . | Clear       | plus 1    | ...       | 0         | 0           |                |
| 39 . . | Clear       | plus 1    | ...       | plus 2    | 0           |                |
| 40 . . | Clear       | plus 1    | 1 l.      | 0         | 0           |                |
| 41 . . | Clear       | plus 1    | 25 l.     | plus 2    | 0           |                |
| 42 . . | Clear       | ...       | 150 l.    | 0         | 0           |                |
| 43 . . | Clear       | ...       | 150 l.    | 0         | 0           |                |
| 44 . . | Clear       | ...       | 50 l.     | 0         | 0           |                |
| 45 . . | Clear       | ...       | 40 l.     | 0         | 0           |                |
| 46 . . | Clear       | ...       | 30 l.     | 0         | 0           |                |
| 47 . . | Clear       | ...       | 29 l.     | 0         | 0           |                |
| 48 . . | Clear       | ...       | 106 l.    | 0         | 0           |                |
| 49 . . | Clear       | ...       | 110 l.    | 0         | 0           |                |
| 50 . . | Clear       | ...       | 60 l.     | 0         | 0           |                |
| 51 . . | 0           | ...       | 5 l.      | plus 1    | 0           |                |
| 52 . . | Clear       | ...       | ...       | 0         | 0           |                |
| 53 . . | Clear       | ...       | ...       | 0         | 0           |                |
| 54 . . | Clear       | ...       | ...       | 0         | 0           |                |
| 55 . . | Clear       | ...       | ...       | 0         | 0           |                |
| 56 . . | Clear       | ...       | 4 l.      | 0         | 0           | 2343341100     |
| 57 . . | Clear       | ...       | 9 l.      | 0         | 0           |                |
| 58 . . | Clear       | plus 1    | ...       | plus      | 0           |                |
| 59 . . | Clear       | plus 1    | 60 l.     | plus      | 0           |                |
| 60 . . | Clear       | plus      | 26 l.     | 0         | 0           |                |

**Treatment.** There is no specific treatment. Adequate nursing, absolute rest and freedom from all excitement is imperative. Hospitalization is to be advised because of better control of laboratory facilities and of the desirability of repeated lumbar puncture. Lumbar puncture was of decided benefit in 10 of our own cases. The patients were brighter, the cranial nerve palsies were improved and headache was often relieved. Opium should be used with care except in the early states, when the pain is severe. The eyes must be protected from the light and from foreign bodies in cases of corneal anesthesia and orbicularis paralyses. Large doses of urotropin have been advised, but there would seem to be little evidence in favor of its use. The fluid intake of the patient should be maintained at a high level. The skin demands attention, as bed-sores are common.

**Conclusion.** It was thought that a statistical tabulation of the symptoms and findings of epidemic encephalitis as revealed in the American literature might be useful, especially in the recognition of the mild or aberrant forms of the disease, which would seem more numerous than is generally appreciated. A basis for the evaluation of symptoms is necessary in a disease the diagnosis of which must be made by exclusion. Either cranial nerve involvement (especially eye muscle disturbances), with or without lethargy or lethargy alone, constitutes sufficient grounds for a diagnosis of epidemic encephalitis in the presence of an epidemic when either is supported by a normal spinal fluid or an atypical spinal fluid in which there is a slight increase in cells or in globulin, or in both, a negative Wassermann, a mild paretic or luetic gold chloride curve and negative bacteriological findings.

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## A CONSIDERATION OF THE AFTER-CARE OF ARRESTED CASES OF ESSENTIAL EPILEPSY.<sup>1</sup>

BY L. PIERCE CLARK, M.D.,  
NEW YORK CITY.

SEVERAL years ago I reported a series of arrested or cured cases of essential epilepsies before this Society.<sup>2</sup> The period of arrest

<sup>1</sup> Read before the American Neurological Association, June, 1920.

<sup>2</sup> The Curability of Idiopathic Epilepsy, with a Report of Twenty-nine Cures, Arch. Int. Med., January, 1912.